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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/676,154	09/29/2003	John Landers	M0656.70098US00	7775

23628 7590 11/06/2009

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EXAMINER	
SALMON, KATHERINE D	

ART UNIT	PAPER NUMBER
1634	

MAIL DATE	DELIVERY MODE
11/06/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/676,154	LANDERS ET AL.	
	Examiner	Art Unit	
	KATHERINE SALMON	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 July 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *149-160,165 and 166* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *149,150,153-160,165 and 166* is/are rejected.

7)☒ Claim(s) *151 and 152* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/17/2009, 8/19/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to papers filed 7/23/2009.

2. Currently claims 149-160 and 165-166 are pending. Claims 1-148, 161-164 have been cancelled.

3. The following rejections to Claims 165-166 are necessitated based upon amendments to the claims and the IDS filed on 8/19/2009 and 7/17/2009. Response to arguments follows.

4. This action is FINAL.

Terminal Disclaimer

5. The terminal disclaimer over US Patent Number 6703228 filed 7/23/2009 was approved on 8/21/2009.

Interview Summary

6. The reply filed on 7/23/2009 is fully responsive and it includes a complete or accurate record of the substance of the in person interview of 7/1/2009.

Information Disclosure Statement

7. The information disclosure statement (IDS) which was submitted on 8/19/2009, 7/17/2009 has been considered. The submissions are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Claim Objections

8. Claims 151-152 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 149-150, 154-158, 160, and 165-166 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lisitsyn et al. (Science 1993 Vol. 259 p. 946) in view of Nikiforov et al. (WO 95/15970 June 15, 1995).

The instant application defines the term "RCG" on p. 16 lines 22-30 as a reproducible fraction of an isolated genome which is composed of a plurality of DNA fragments (lines 22-23).

With regard to Claims 149-150 and 165-166, Lisitsyn et al. teaches a method of preparing a randomly primed PCR derived RCG using at least one PCR primer (abstract and p. 946 3rd column 1st 2 paragraphs). Lisitsyn et al. teaches that in RDA (representational difference analysis) DNA complexity of tester and driver genomes are reduced so that only a subset of the whole genome is represented (abstract and p. 946 3rd column 1st 2 paragraphs). Lisitsyn et al. teaches that the complexity can be reduced by 55 times. Therefore in a human genome of 3×10^9 the RCG represents less than 1.8% of the starting genome.

Lisitsyn et al. teaches that the amplicons are reduced by addition of a random PCR primer and amplified (Figure 1).

With regard to Claim 154, Lisitsyn et al. teaches that the PCR primer is an adapter primer (947 1st paragraph).

With regard to Claims 157-158, Lisitsyn et al. teaches a method of preparing a randomly primed PCR derived RCG using at least one PCR primer (abstract and p. 946 3rd column 1st 2 paragraphs). Lisitsyn et al. teaches that in RDA (representational difference analysis) DNA complexity of tester and driver genomes are reduced so that only a subset of the whole genome is represented (abstract and p. 946 3rd column 1st 2 paragraphs). Lisitsyn et al. teaches that the complexity can be reduced by 55 times. Therefore in a human genome of 3 X 10^9 the RCG represents less than 1.8% of the starting genome. Lisitsyn et al. teaches the use of tumor cells (figure 4).

Lisitsyn et al. teaches that the amplicons are reduced by addition of a random PCR primer and amplified (Figure 1).

With regard to Claim 160 Lisitsyn et al. teaches that the PCR primer is an adapter primer (947 1st paragraph).

However, Lisitsyn et al. does not teach method steps of using such RCG fragments to detect SNPs or to genotype.

Nikiforov et al. teaches a method of using a solid support immobilized with nucleic acid molecules for polymorphic analysis and sequencing (e.g. genotyping) (abstract).

With regard to Claim 149, 157, and 165-166, Nikiforov et al. teaches a method wherein a single stranded PCR product is prepared before hybridization (p. 14 lines 17-18). However, ordinary artisan would be motivated to use the RCG amplified segment of Lisitsyn et al. in replacement of Nikiforov et al. PCR derived genetic product, because Lisitsyn et al. teaches PCR amplified samples could be used in methods of genetic

analyses. Nikiforov et al. teaches that this complex can be used to detect SNP alleles (p. 31 lines 15-18).

Nikiforov et al. teaches hybridizing the PCR derived complex to capture probes (e.g. arrayed panel of oligonucleotides) to detect the specific products (p. 14 lines 13-15). Nikiforov et al. teaches that the hybridization patterns determined the presence or absence of the SNP (p. 31 lines 15-18).

With regard to Claims 155-156, Nikiforov et al. teaches that the length of the nucleic acids can be at least 12 nucleotides (e.g. between 10 and 25 nucleotides) (p. 8 lines 5-7).

With regard to Claim 166, Nikiforov et al. teaches a method wherein a single stranded PCR produce is prepared before hybridization (p. 14 lines 17-18). Therefore Nikiforov et al. teaches preparing a PCR derived complex from genomic DNA. Nikiforov et al. teaches that the practice can be used to sequence (p. 15 lines 35-38) and therefore Nikiforavo et al. teaches that the sample can be genotyped.

Nikiforov et al. teaches hybridizing the PCR derived complex to capture probes (e.g. arrayed panel of oligonucleotides) to detect the specific products that have the presence or absence of a SNP (p. 14 lines 13-15 and p. 31 lines 15-18). Therefore the panel of oligonucleotides comprises alleles (oligonucleotides) that are specific for a particular SNP. Nikiforov et al. teaches that the PCR complex hybridizes to the oligonucleotides (p. 31 lines 15-18) and therefore the oligonucleotides comprise a SNP allele which is specific for the PCR complex.

Therefore it would be prima facie obvious to modify the method of Lisitsyn et al. to further use the array of Nikiforov et al. which involves detecting SNPs using a microarray using PCR amplified fragments. It would have been obvious to one of ordinary skill in the art at the time the invention was made to use randomly primed PCR derived RCG fragments in a method of using PCR product complexes to hybridize to oligonucleotides immobilized on an array to detect SNPs with a reasonable expectation of success because the prior art of Lisitsyn et al suggest that randomly-primed PCR derived RCG fragments may be successfully used in genetic analyses such as detection of polymorphism (p. 950 1st column last paragraph) such as those taught by Nikiforov et al.

11. Claims 153 and 159 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lisitsyn et al. (Science 1993 Vol. 259 p. 946) and Nikiforov et al. (WO 95/15970 June 15, 1995) as applied to 149-150, 154-158, 160, and 165-166 and in view of Cheung et al. (Proceedings National Academy Science 1996 Vol 93 p. 14676).

With regard to Claims 153 and 159, Lisitsyn et al. and Nikiforov et al. teaches a method of preparing randomly primed PCR derived RCG, contacting SNP ASOs immobilized on a surface with RCG and determining the presence or absence of a SNP allele in the RCG, but do not teach that the PCR primer is a DOP-PCR primer.

With regard to Claims 153 and 159, Cheung et al. teaches using DOP-PCR amplification to produce genomic fragments (p. 14676 2nd column DOP amplification). Cheung et al. teaches that the PCR reaction uses a DOP primer, which is degenerative

(p. 14676 2nd column DOP amplification). Cheung et al. teaches that arbitrary portions of the DNA sequences are amplified by this method (p. 14676 2nd column 1st paragraph).

Therefore it would be prima facie obvious to one of ordinary skill in the art at the time of filing to modify the method of Lisitsyn et al and Nikiforov et al. to generate RCGs using any number of randomly primed PCR primers including DOP-PCR primers as taught by Cheung et al. Cheung et al. suggests that the ordinary artisan would be motivated to try using the DOP-PCR amplified samples (e.g. the randomly-primed PCR derived RCG fragments) in other PCR based genetic analyses such as sequencing and single stranded conformation polymorphism (p. 14678 2nd column 1st paragraph). It would have been obvious to one of ordinary skill in the art at the time the invention was made to choose form a finite number of predictable randomly primed PCR primers, such as DOP PCR, with a reasonable expectation of success of amplifying a randomly primed amplicon of the genomic material.

12. Claims 165-166 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cheung et al. (Proceedings National Academy Science 1996 Vol 93 p. 14676) in view of Nikiforov et al. (WO 95/15970 June 15, 1995).

The instant application defines the term “RCG” on p. 16 lines 22-30 as a reproducible fraction of an isolated genome which is composed of a plurality of DNA fragments (lines 22-23).

With regard to Claim 165, Cheung et al. teaches using DOP-PCR amplification to produce genomic fragments (p. 14676 2nd column DOP amplification). Cheung et al. teaches that the PCR reaction uses a DOP primer, which is degenerative (p. 14676 2nd column DOP amplification). Cheung et al. teaches that arbitrary portions of the DNA sequences are amplified by this method (p. 14676 2nd column 1st paragraph).

Cheung et al. characterizes the DOP-PCR method as whole genome amplification, however, the methodology of Cheung et al. actually teaches that only portions of the genome is amplified and therefore less the whole genome is amplified. Cheung et al. teaches that 200 to 1000 bp fragments were produced (p. 14677 1st column 2nd paragraph). Cheung et al. teaches that only 1 of every 10 200-1000 bp pairs stretches of the human genome is amplified (p. 14678 2nd column last paragraph). Cheung et al. teaches that the human genome is about 3 X 10^9 bp. Therefore Cheung et al. teaches amplification of less than the whole genome. Further Cheung et al. teaches that the fractions are amplified and a plurality of fragments are produced(p. 14676 2nd column 1st paragraph), therefore Cheung et al. teaches RCG fragments as defined by the instant specification because Cheung et al. teaches amplification of less than the entire genome.

Cheung et al suggest that DOP-PCR amplified samples (e.g. the randomly-primed PCR derived RCG fragments) may be successfully used in genetic analyses such as sequencing and single stranded conformation polymorphism. However, Cheung et al. does not teach method steps of using such RCG fragments to detect SNPs or to genotype.

Specifically, Cheung et al. teaches using a DOP primer with a 6 nucleotide tag on the 3' end (p. 14676 last full paragraph). The instant specification discloses that the complexity of the resultant product when using 6 nucleotide tag on the 3' end is extremely high due to the short length, whereas the complexity of the genome is significantly reduced using 7 or 8 nucleotides on the 3' end (p. 73 liens 17-24). Cheung et al. teaches that 200 to 1000 bp fragments were produced (p. 14677 1st column 2nd paragraph). Cheung et al. teaches that only 1 of every 10 200-1000 bp pairs stretches of the human genome is amplified (p. 14678 2nd column last paragraph). Cheung et al. teaches that the human genome is about 3×10^9 bp. Therefore one would expect the complexity of the Cheung et al. genome of about 20% in the samples in which 200 bp fragments are produced and higher complexity as the bp fragments get larger. Therefore Cheung et al. teaches that at least about 10% is amplified and as much as 20% is amplified. As such the reduced complexity of Cheung et al. would be less than 30% of genomic material (e.g. about 20%).

Nikiforov et al. teaches a method of using a solid support immobilized with nucleic acid molecules for polymorphic analysis and sequencing (e.g. genotyping) (abstract).

With regard to Claim 165, Nikiforov et al. teaches a method wherein a single stranded PCR product is prepared before hybridization (p. 14 lines 17-18). However, ordinary artisan would be motivated to use the RCG amplified segment of Cheung et al. in replacement of Nikiforov et al. PCR derived genetic product, because Cheung et al. teaches that these DOP-PCR amplified samples could be used in methods of genetic

analyses. Nikiforov et al. teaches that this complex can be used to detect SNP alleles (p. 31 lines 15-18).

Nikiforov et al. teaches hybridizing the PCR derived complex to capture probes (e.g. arrayed panel of oligonucleotides) to detect the specific products (p. 14 lines 13-15). Nikiforov et al. teaches that the hybridization patterns determined the presence or absence of the SNP (p. 31 lines 15-18).

With regard to Claim 166, Nikiforov et al. teaches a method wherein a single stranded PCR produce is prepared before hybridization (p. 14 lines 17-18). Therefore Nikiforov et al. teaches preparing a PCR derived complex from genomic DNA. Nikiforov et al. teaches that the practice can be used to sequence (p. 15 lines 35-38) and therefore Nikiforavo et al. teaches that the sample can be genotyped.

Nikiforov et al. teaches hybridizing the PCR derived complex to capture probes (e.g. arrayed panel of oligonucleotides) to detect the specific products that have the presence or absence of a SNP (p. 14 lines 13-15 and p. 31 lines 15-18). Therefore the panel of oligonucleotides comprises alleles (oligonucleotides) that are specific for a particular SNP. Nikiforov et al. teaches that the PCR complex hybridizes to the oligonucleotides (p. 31 lines 15-18) and therefore the oligonucleotides comprise a SNP allele which is specific for the PCR complex.

Therefore it would be prima facie obvious to modify the method of Nikiforov et al. which involves detecting SNPs using a microarray using PCR amplified fragments of DNA by using randomly-primed PCR derived RCG fragments taught by Cheung et al. Cheung et al. suggests that the ordinary artisan would be motivated to try using the

DOP-PCR amplified samples (e.g. the randomly-primed PCR derived RCG fragments) in other PCR based genetic analyses such as sequencing and single stranded conformation polymorphism (p. 14678 2nd column 1st paragraph). It would have been obvious to one of ordinary skill in the art at the time the invention was made to use randomly primed PCR derived RCG fragments in a method of using PCR product complexes to hybridize to oligonucleotides immobilized on an array to detect SNPs with a reasonable expectation of success because the prior art of Cheung et al suggest that DOP-PCR amplified samples (e.g. the randomly-primed PCR derived RCG fragments) may be successfully used in genetic analyses such as sequencing and single stranded conformation polymorphism.

Response to arguments

The reply traverses the rejection. A summary of the arguments presented in the reply is set forth below, with response to arguments following.

The reply asserts that although he applicant disagrees with the rejection in order to advance prosecution the claims have bee amended to recite the limitation that the RCG contains less than 30% of genomic material present in the whole genome (p. 5 last paragraph).

This argument has been fully reviewed but has not been found persuasive.

Specifically, Cheung et al. teaches using a DOP primer with a 6 nucleotide tag on the 3' end (p. 14676 last full paragraph). The instant specification discloses that the complexity of the resultant product when using 6 nucleotide tag on the 3' end is

extremely high due to the short length, whereas the complexity of the genome is significantly reduced using 7 or 8 nucleotides on the 3' end (p. 73 liens 17-24). Cheung et al. teaches that 200 to 1000 bp fragments were produced (p. 14677 1st column 2nd paragraph). Cheung et al. teaches that only 1 of every 10 200-1000 bp pairs stretches of the human genome is amplified (p. 14678 2nd column last paragraph). Cheung et al. teaches that the human genome is about 3 X 10^9 bp. Therefore one would expect the complexity of the Cheung et al. genome of about 20% in the samples in which 200 bp fragments are produced and higher complexity as the bp fragments get larger. Therefore Cheung et al. teaches that at least about 10% is amplified and as much as 20% is amplified. As such the reduced complexity of Cheung et al. would be less than 30% of genomic material (e.g. about 20%).

Conclusion

13. Applicant's submission of an information disclosure statement under 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p) on 8/19/2009 prompted the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 609.04(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to KATHERINE SALMON whose telephone number is (571)272-3316. The examiner can normally be reached on Monday - Friday 9AM-530PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on (571) 272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Katherine Salmon

/Sarae Bausch/
Examiner, Art Unit 1634